Ph.D. SYNOPSIS (2017-18)

RESEARCH STUDENT	**Mr. SHAIKH NASHEER SHADULLA**
MAIL ID.	nasheershaikh@gmail.com
MOBILE NO.	**+91 9860821659 / +91 8421777027**
CATEGORY	OPEN
SUBJECT	PHARMACEUTICAL SCIENCES
FACULTY	SCIENCE & TECHNOLOGY
Ph.D. SYNOPSIS TITLE	**FORMULATION, DEVELOPMENT AND EVALUATION OF NANOSPONGES FOR TOPICAL APPLICATION**
RESEARCH GUIDE	**Dr. NAGOBA S. N.**
MAIL ID.	nagobashivraj@gmail.com
MOBILE NO.	**+91 9637908901**
DESIGNATION	ASSOCIATE PROFESSOR AND HEAD, DEPT. OF PHARMACEUTICS, CHANNABASWESHWAR PHARMACY COLLEGE, KAVA ROAD, LATUR.
RESEARCH CENTRE	SCHOOL OF PHARMACY, S.R.T.M.UNIVERSITY, NANDED.
UNIVERSITY	SWAMI RAMANAND TEERTH MARATHWADA UNIVERSITY, NANDED-431606, (MAHARASHTRA STATE), INDIA.
DATE OF R.A.C.	**23/11/2017**
DATE OF R.R.C.	**31/03/2018**
PLACE OF R.R.C.	**S.R.T.M UNIVERSITY, NANDED.**

"FORMULATION, DEVELOPMENT AND EVALUATION OF NANOSPONGES FOR TOPICAL APPLICATION"

A SYNOPSIS SUBMITTED FOR THE REGISTRATION OF *DEGREE OF*

DOCTOR OF PHILOSOPHY

In the Faculty of Pharmaceutical Sciences & Technology

Submitted

By

Mr. SHAIKH NASHEER SHADULLA
M. Pharm.

Under the Guidance of

Dr. NAGOBA S. N.
M. Pharm. Ph.D.
Associate Professor and Head,
Dept. of Pharmaceutics,
CHANNABASWESHWAR PHARMACY COLLEGE, LATUR

Swami Ramanand Teerth Marathwada University,

Nanded-431606, (Maharashtra State), India.

(2017-2018)

INDEX

SR.NO.	CONTENT	PAGE NO.
01	ABSTRACT OF PROPOSED WORK PLAN	04
02	INTRODUCTION	05
03	REVIEW OF LITERATURE AND DEVELOPMENT IN THE SUBJECT	11
04	OBJECTIVES OF RESEARCH	15
05	MATERIALS & METHODOLOGY TO BE ADOPTED	16
06	IMPORTANCE OF STUDY	18
07	PROPOSED WORK PLAN	20
08	REFERENCES	21

1. Abstract of proposed work plan/ problem:

Nanosponges are tiny mesh like novel class hyper crosslinked polymer based colloidal structures in which large variety of drug molecules encapsulated within its core. They are having the size of a virus with an average diameter below 1µm. Nanosponges are effective drug carriers which possess higher drug loading capacities compared to other nanocarriers. So they are useful to increase stability, solubility, bioavailability and target or delayed release of drug also it is helpful in solving toxicity problems of drugs. They are able to load both hydrophilic and lipophilic drugs of various categories. Nanosponges are three dimensional network (3D) or scaffold with highly porous nature. It can deliver the drugs through various routes like oral, topical, parenteral etc. and used as biocatalyst in the delivery of enzymes, proteins, vaccines and antibodies.

The purpose of this study is to increase solubility and bioavailability also to decrease toxicity of drug by using nanosponges hydrogel formulation. This will be done by preparing nanosponges hydrogel and characterized by DSC, XRD, FTIR, Entrapment efficiency, Zeta potential etc. Further these nanosponges will be dispersed in hydrogel by using suitable gelling agent and the hydrogel will be evaluated by viscosity, pH, Spreadability, *in vivo* and *in vitro* studies.

Key words: nanosponges; hydrogel*; in vivo*; *in vitro;* crosslinkers; topical application

2. Introduction:

Therapeutic effectiveness of drug depends upon the bioavailability and in turn upon the solubility. In pharmaceutical industries near about 70% drugs which are investigated are poorly water soluble and belongs to the BCS class II category.[1] Oral delivery of drugs is preferred for those drugs which are having problems such as poor bioavailability, poor water solubility and narrow absorption window. To overcome these limitations various drug delivery systems are used. One of the most important revolution in this field is Nanotechnology.[2] Nanotechnology is defined as manufacturing and conversion of materials at nanoscale level that create final products which shows novel properties. It includes various formulations like nanoparticles, nanocapsules, nanospheres, nanosponges, nanosuspensions, nanocrystals etc. Nanoparticles having applications such as biocompatible materials, textile functionalization and coating against microbial degradation, drug delivery, DNA delivery etc. nanoparticles are available in various dosage forms like polymeric nanoparticles , solid lipid nanoparticles, nanoemulsions, nanosponges, carbon nanotubes, dendrimers etc. [3]

Nanosponges are tiny mesh like novel class hyper crosslinked polymer based colloidal structures in which large variety of drug molecules encapsulated within its core. They have been a proved spherical colloidal nature, reported to have a very high solubilization capacity for BCS class II (poorly soluble drugs) by their inclusion and non-inclusion behaviour. They have been recently developed and proposed for drug delivery. It can be solubilize poorly water soluble drugs and provide prolonged release as well as increasing drugs bioavailability. Nanosponges can load both hydrophilic and hydrophobic drug molecules because of their inner hydrophobic cavities and external hydrophilic branching, thereby offering flexibility. They are more like a (3D) three dimensional network or scaffold. The backbone is a long length of polyester which is mixed in solution with small molecules called crosslinkers that act as tiny grappling hooks to fasten different parts of the polymer together. It shows a marked advantage in comparison with the common nanoparticles. Indeed, it can be easily regenerated by different treatments, such as washing with eco-compatible solvents, stripping with moderately inert hot gases, mild heating or changing pH or ionic strength. So nanosponges have been already employed in different applied fields, such as cosmetics and pharmaceutical sectors. Compared to many other nanoscale drug delivery systems, the engineering capacity of nanosponges is due to the relatively simple chemistry of its polyesters and crosslinking

peptides. They are water soluble but does not breakup chemically in water. They also mix with water and use it as a transport fluid. They are used to mask unpleasant odour and taste, to convert liquid substances to solids. The chemical linkers enable the nanosponges to bind preferentially to the target site.

They are solid in nature and have been found to be safe for oral and invasive routes of administration and so that they could serve as a potential carrier for drug delivery system. The small shape of nanosponges enables the pulmonary and parenteral delivery successfully. For oral administration, the complexes may be dispersed in a matrix of excipients, diluents, lubricants and anti-caking agents suitable for the preparation of capsules or tablets, for parenteral administration the complex may be simply carried in sterile water, saline or other aqueous solutions and for topical administration they can be effectively incorporated into hydrogel. They are encapsulating nanoparticles which encapsulate the drug molecules within its core and having the size of a virus with an average diameter below 1µm.[4,5,6,7]

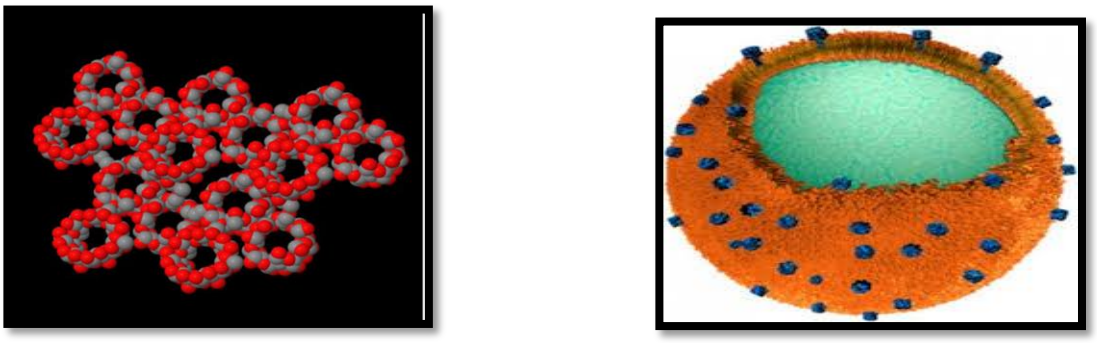


Figure 1: Molecular structure of nanosponges

Advantages of Nanosponges: [8,9,10,11,12]

- It provides site specific and targeted drug delivery at predetermined rate.
- They are non-mutagenic, non-irritant and non-toxic.
- Nanosponges protect the active ingredients from decomposition or degradation.
- It is cost effective.
- It masks the unpleasant flavors of drug substances.
- Immiscible liquids can be incorporated in nanosponges.
- Regeneration of nanosponges can be carried out by washing with eco-compatible solvents, stripping with inert hot gases, mild heating, changing pH or ionic strength.
- They are easy to scale up.
- It helps to improve stability, elegance and formulation flexibility.

Disadvantages of nanosponges:

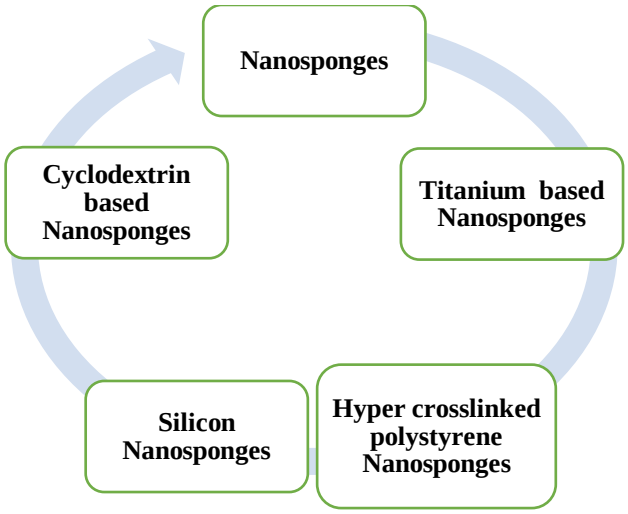
- They are depends upon drug loading capacity.
- Only small molecules are formulated in nanosponges.

Characteristic features of nanosponges: [8,9,10,11,12,13,14]

- They are having dimensions 1 µm or less with tunable polarity of the cavities.
- Nanosponges with different specific sizes can be synthesized by changing the crosslinker to polymer ratio.
- They exhibit both paracrystalline and crystalline forms which are depend upon process condition.
- Nanosponges are porous particles and insoluble in most organic solvents.
- They are stable at temperature up to 130^0C.
- They are stable at pH range 1-11.
- They can be reproduced by simple thermal desorption, extraction with solvents, by using microwaves and ultrasounds.
- The 3 dimensional structure of nanosponges helps to capture, transportation and selective release of variety of substances.
- Nanosponges can bind preferably to target site because of their capacity to link with different functional groups.
- They can form inclusion and non-inclusion complexes.

Types of nanopsonges: [14,15]

Nanosponges are of following types:



Chemicals used in preparation of Nanosponges:

There are various polymers and crosslinkers used in the formulation of nanosponges which are as follows;

1. **Polymers:** Hyper crosslinked Polystyrenes Cyclodextrines and its derivatives Copolymers like Poly(valerolactoneallylvalerolactone) and Poly(valerolactoneallylvalerolactoneoxepanedione) Ethyl cellulose, PVA, etc.
2. **Crosslinkers:** Diphenyl carbonate, Diarylcarbonates, Diisocyanates, Pyromellitic anhydride, Carbonyldiimidazoles, Epichloridrine, Glutarldehyde, Carboxylic acid dianhydrides, Dichloromethane, etc.
3. **Apolar solvents:** Ethanol, Dimethylacetamide, Dimethyl formamide, Dimethyl sulfoxide, etc.

Factors affecting nanosponges formulation:[16,17]

The ideal nanosponges formulations properties altered by effect of various factors. Some factors are explained as follows:

1. Type of drug:

The drug molecules encapsulated in nanosponges by inclusion and non-inclusion complexes should have following ideal characteristics:

i. Solubility of drug in water is less than 10 mg/ml.
ii. The molecular weight of drug between 100 to 400 gm /mole.
iii. The drug molecule should not contain more than five condensed rings.
iv. The melting point of drug should be less than 250^0C.

2. Type of polymers & crosslinkers:

The type of polymers and crosslinkers used in the preparation of nanosponges decides the quality of preparation and performance of nanosponges. Crosslinkers are used to transform molecular nanocavities into three dimensional nanoporous structures. Also by changing the degree of crosslinking that is hydrophilic or hydrophobic components can be formulated which are able to form targeted compounds. Also crosslinkers are responsible to modify rate of drug release, enhance drug absorption across biological barriers.

3. Medium of interaction:

The interaction of nanosponges with drug is strongly depends upon medium used that is hydrophilic and hydrophobic. This interaction is depend on polarity, size and structural properties of drug.

4. Temperature:

Temperature changes affect the stability of nanosponges formulations. An increase in temperature decreases the magnitude of stability. This is happened due to decrease in interaction forces of nanosponges. So it is very important to keep control over temperature during preparation of nanosponges.

5. Method of preparation:

The method of preparation can affect the nanosponges formulation, because the drug loading capacity and complexation depends upon the preparation method. Also it includes the polymer and drug interaction.

6. Degree of substitution:

The type, number and position of substituent on parent molecule can affect the nanosponges formation as well as its complexation.

Applications of nanosponges: [17]

- Nanosponges have many applications in pharmaceutical field. Some of them are as follows:
- In solubility enhancement.
- In drug delivery.
- For protein delivery.
- In enzyme immobilization.
- As a carrier for delivery of gases.
- As protective agent for photo degradation.
- Modulating drug release.
- Effective drug carriers.

Other Applications

- Biomedical Application
- Analytical Application
- For Hydrogen storage
- In Agriculture
- In Floriculture
- In Food Industry
- For water Purification
- For Oil Cleaning
- As Novel flame Retardants
- Against pore forming Toxins and superbug infections,
- Micro patterning of Mammalian cell

3. Review of Literature and Development in the subject (Previous work done in the relevant area):

1. Gangadharappa H.V. *et al.* (2017): [18]

This study proposed to increase the solubility of Celecoxib using β-cyclodextrin and NN-methylene bisacrylamide Nanosponges hydrogel formulation. Nanosponges of celecoxib were prepared and characterized by differential scanning colorimetry, X-ray diffractometry, FT-IR analysis and evaluated by Zeta-potential and Polydispersity index and drug entrapment efficiency. Further, celecoxib nanosponges were dispersed in 1% carbopol 934 hydrogel and the gel was evaluated for its viscosity, pH, spreadability, *in vitro* diffusion. *In vivo*, pharmacokinetic and skin irritation studies in rats.

2. Prathima Srinivas *et al*. (2013): [19]

This study proposed the preparation of controlled release Voriconazol nanosponges for topical and oral delivery. Nanosponges were prepared using three different polymers ethyl cellulose, Poly (methyl methacrylate) and Pluronic F-68 (poloxamer 188) successfully using PVA as surfactant by emulsion solvent evaporation method. The physical characteristics of the nanosponges as well as the drug entrapment efficiency of the nanosponges were investigated. Particle size analysis and surface morphology of nanosponges were performed. The scanning electron microscopy of nanosponges showed that they were spherical in shape and spongy in nature. These nanosponge formulations were prepared as hydrogel using carbopol 971P and studied for pH, viscosity, in vitro drug release, antimicrobial activity. Antifungal activity of the optimized formulations was evaluated *in vivo* in Male Wistar rats in comparison with marketed Flucos gel. The optimized nanosponge formulations were selected for preparing nanosponge tablets for controlled drug delivery by oral route. These tablets were prepared using microcrystalline cellulose and were evaluated for hardness, friability, drug content and *in vitro* drug release studies.

3. Patil Bhagyashree Subhash *et al*. (2016): [20]

In this work researcher prepared controlled release Artesunate nanosponges for topical and oral delivery. Nanosponges were prepared using three different polymers ethyl cellulose, Poly

(methyl methacrylate) and Pluronic F-68 (poloxamer 188) successfully using PVA as surfactant by emulsion solvent evaporation method. The physical characteristics of the nanosponges as well as the drug entrapment efficiency of the nanosponges were investigated. Particle size analysis and surface morphology of nanosponges were performed.

4. Khalid A. Ansari *et al*. (2011): [21]

This study is proposed to increase the solubility, stability and permeation of resveratrol by preparing cyclodextrin based nanosponges. Nanosponges were prepared by reacting cyclodextrin with cyclodextrin with cross-linker such as carbonyldiimidazole. This study aimed at formulating complexes of resveratrol with β-cyclodextrin nanosponges in different weight ratios. DSC, FTIR and XRPD studies confirmed the interaction of resveratrol with nanosponges. XRPD showed that the crystallinity of resveratrol decrease after encapsulation. The particle sizes of resveratrol-loaded nanosponges are in between 400 to 500 nm. Zeta potential is sufficiently high to obtain a stable colloidal nanosuspension. The in vitro release and stability of resveratrol complex were increased compared with plain drug. The permeation study indicates that the resveratrol NS formulation showed good permeation in pigskin. The accumulation study in rabbit mucosa showed better accumulation of resveratrol NS formulation than plain drug. These results signify that resveratrol NS formulation can be used for buccal delivery and topical application.

5. Kamla P. *et al* (2011): [22]

The present study was carried out to prepare polymeric nanosponges of econazole nitrate and topical hydrogel formulation. Nanosponges prepared by emulsion solvent diffusion method were evaluated for various physicochemical parameters and in vitro drug release. The nanosponges of econazole nitrate were studied by SEM. The nanosponge formulated using PVA:EC (3:2) displayed highest in vitro release after 12 h in phosphate buffer (pH 6.8) that fitted matrix model. Selected nanosponge was formulated as Carbopol 934 NF hydrogel using varying concentrations of permeation enhancers propylene glycol and N-methyl-2-pyrrolidone. The econazole nitrate nanosponge-loaded hydrogels were evaluated for pharmacotechnical properties and irritation studies on rat skin. On the basis of various

evaluation parameters the preparation with best results after stability studies were selected for drug delivery.

6. Vidya viswanad *et al* (2015): [23]

In this, researcher reported that cephalexin is not available as topical formulation, cephalexin was formulated into nanosponge loaded hydrogel. Nanosponges of cephalexin were prepared using hydroxyl ethyl cellulose and poly vinyl alcohol by emulsion solvent evaporation method. The particle size and entrapment efficiency was found in the range of 200- 400 nm and 88.5%- 95.6% respectively. Based on the characterization, nanopsonges with high entrapment efficiency and least particle size (NS2) was selected for hydrogel formulation. Hydrogels were prepared by using carbopol 934 with varying concentration of penetration enhancer (propylene glycol) and various evaluation studies were carried out. The *in vitro* release studies revealed that the formulation with higher concentration of penetration enhancer (15% propylene glycol) showed greater drug release and also good permeation.

7. Prashant Kesharwani *et al* (2017): [24]

This study proposed that Cyclodextrin based nanosponges are prepared for increasing oral solubility of poorly water-soluble medications such as nifedipine. DLS studies confirmed particle size in the range of 400-500 nm with monodisperse size distribution. TEM measurement established spherical shape and size range of the nanosuspension. SEM photomicrograph confirmed porous structure of placebo nanosponges while drug loaded nanosponge formulation revealed solid surface. FTIR studies established no drug-polymer interaction. DSC thermograms showed molecular level dispersion of drug in nanosponges. *In vitro* drug release exhibited a burst release for first fourth hour and delivered drug in sustained manner for subsequent 24 hours. When encapsulated within nanosponges, oral bioavailability of nifedipine was enhanced in comparison to control formulation. The fabricated nanosponges displayed admirable stability under normal and stress conditions. % Drug entrapment encountered a slight decline (77.33±1.62% to 74.13±1.47%) during storage while % drug release from initial batch was almost identical when compared with stored nanosponges.

8. D. Lembo *et al* (2013): [25]

In this work, new carboxylated cyclodextrin-based nanosponges were prepared using Acyclovir drug. Physical evaluations were done by FTIR, DSC, XRD. In vitro release studies showed the release kinetics of Acyclovir from Carb-NS to be prolonged in comparison with those observed with NS, with no initial burst effect. The NS uptake into cells was evaluated using fluorescent Carb-NS and revealed the nanoparticle internalisation. Enhanced antiviral activity against a clinical isolate of HSV-1 was obtained using Acyclovir loaded in Carb-NS.

9. S. Swaminathan *et al* (2007): [26]

This study proposed that, nanosponges of b CD improved the solubility of itraconazole many folds and addition of an auxiliary component copolyvidonum enhanced the solubility further. Due to more solubilization, the bioavailability of itraconazole can be expected to be more as compared to plain drug. Thus the objective of the work was achieved using a ternary system of nanosponges and copolyvidonum. nanosponges of β-CD improved the solubility of itraconazole many folds and addition of an auxiliary component copolyvidonum enhanced the solubility further. Due to more solubilization, the bioavailability of itraconazole can be expected to be more as compared to plain drug. Thus the objective of the work was achieved using a ternary system of nanosponges and copolyvidonum.

4. Aim & Objectives of Research/ Proposed Hypothesis:

Aim: Formulation, Development and Evaluation of Nanosponges for Topical Application.

Objectives of the Research Work:

- To prepare, optimize, characterize Nanosponges system for Topical application System and set parameters that can serve as quality control tool.
- To perform Preformulation studies of selected API.
- To prepare and evaluate drug loaded nanopsonges hydrogel.
- To improve the efficacy, drug loading capacity and biocompatibility of drug by formulating in nanosponges.
- To minimize the toxicity and increase the stability of drug by encapsulating in nanosponges system.
- To optimize the developed formulation.
- Physicochemical, *in-vitro* and *in-vivo* evaluation of optimized formulation.
- To study stability of optimized formulation.
- To improve the solubility of drug.

5. Materials & Methodology to be adopted:

1. Extensive Literature review

2. Selection and Collection of drug & excipients

Selection of drug: drug will be selected based on following criteria:

i. Solubility of drug in water is less than 10 mg/ml.
ii. The molecular weight of drug between 100 to 400 gm/mole.
iii. The drug molecule should not contain more than five condensed rings.
iv. The melting point of drug should be less than 250^0C.

Drug: Crisaborole or Efinaconazole or Tavaborole, etc

Selection of polymer: polymer will be selected from following:

Hyper crosslinked Polystyrenes Cyclodextrins and its derivatives Copolymers like Poly(valerolactoneallylvalerolactone) and Poly(valerolactoneallylvalerolactoneoxepanedione) Ethyl cellulose, PVA etc.

Selection of Crosslinkers: Crosslinkers will be selected from following:

Diphenyl carbonate, Diarylcarbonates, Diisocyanates, Pyromellitic anhydride, Carbonyldiimidazoles, Epichloridrine, Glutarldehyde, Carboxylic acid dianhydrides, Dichloromethane etc.

Selection of apolar solvent: solvent will be selected from following:

Ethanol, Dimethyl acetamide, Dimethyl formamide, Dimethyl sulfoxide, etc.

3. Experimental work

A. Preformulation studies:

- Procurement of drug samples and excipients
- Organoleptic properties
- Solubility analysis
- Melting point
- Partition coefficient
- UV spectral analysis
- FT-IR spectral analysis
- Differential Scanning Calorimetry (DSC)
- X-Ray Diffraction (XRD) analysis

- Drug excipients compatibility Study

4. Formulation development

Preparation of Nanosponges

Nanosponges will be prepared by using following methods:

1. Emulsion solvent diffusion method
2. Hyper cross linked β cyclodextrins
3. Ultra sound assisted method

Preparation of Nanosponges Hydrogel

Nanosponges Hydrogel will be prepared by using suitable gelling agent e.g. Carbopol, HPMC, HEC etc. with suitable penetration enhancer like propylene glycol etc.

Optimization of drug-loaded nanosponges & nanosponges hydrogel

5. Evaluation of drug-loaded Nanosponges

- Particle Size and Zeta Potential measurement
- Surface morphology by Scanning Electron Microscopy
- Entrapment Efficiency
- Physical parameters
- FT-IR
- XRD
- Transmission Electron Microscopy(TEM)

Evaluation of drug-loaded Nanosponges Hydrogel

- Homogeneity
- Drug content
- Viscosity
- pH
- spreadability

***In Vitro* drug release study**

***In Vivo* studies**

In vivo studies will be conducted using guinea pig or albino/wistar rats.

Skin irritation studies

Stability Studies as per ICH guideline

6. Importance of study/ Society application:

►International status:

Nanosponges are one of the best in class nanocarriers. Mainly nanosponges are used for topical delivery of drugs. So recent research also focuse on preparation of nanosponges globally. Recently nanosponges hydrogel of celecoxib was prepared to improve the solubility and bioavailability of Celecoxib which is an extremely lipophilic and poorly water soluble NSAID drug, which is also having GIT side effects. Its bioavailability is 40% when administered orally. Nanosponges hydrogel of celecoxib was prepared by using β-cyclodextrin and NN-methylene bisacrylamide. Nanosponges of celecoxib were prepared and characterized by various parameters. Further, celecoxib nanosponges were dispersed in 1% carbopol 934 hydrogel and the gel was evaluated for its viscosity, pH, spreadability, *in vitro* diffusion. *In vivo*, pharmacokinetic and skin irritation studies conducted on rats.[19]

Another preparation of nanosponges hydrogel of cephalexin was available to increase drug release and stability. Cephalexin is first generation cephalosporin antibiotic used in the treatment of skin, soft tissue infection, diabetic foot infection and urinary tract infection.

Nanosponges of cephalexin were prepared by using hydroxyl ethyl cellulose and polyvinyl alcohol by emulsion solvent evaporation method. Which were formulated in hydrogel by using Carbopol and propylene glycol as penetration enhancer. And the evaluation results shown that increase in permeability and stability of drug. [23]

►National Status:

National status also focus on preparation of nanosponges hydrogel. In that first nanosponges hydrogel of isoniazid are available. It includes preparation of isoniazid loaded nanosponges for topical delivery to prolong the drug release and useful in treatment of cutaneous tuberculosis. The method used for preparation of nanosponges was emulsion solvent evaporation method using ethyl cellulose, polyvinyl alcohol. Nanosponges were evaluated for different parameters and optimized preparation was selected for formulating nanogels using various gelling agents like Carbopol, HPMC and evaluated for various parameters and select the formulation which gives best results in terms of sustain drug release and to reduce systemic toxicity.

►Significance/need of the study:

- Topical Infections have been increasing in incidence in the human population over the last 15 years or so, largely as a consequence of increased numbers of cancer and immune compromised patients, who are at risk owing to weakened immune systems and chronic nature of the disease.
- Systemic infections are more serious as they are usually more difficult to diagnose, are chronic in nature, and in some cases, can become life-threatening.
- Nanosponges are mainly for Topical drug delivery.
- It is very much suitable for topical agents.
- Nanosponge is a nano sized particle, has larger surface area, thereby the penetration is high when compared to other conventional products.
- Low solubility drugs formulated as Nanosponge may increase the solubility thereby increase the release and activity.
- Stability of Nanosponge is higher than most of the novel formulation.
- Other benefits such as dose reduction, reduced frequency of administration and avoiding systemic side effects.
- It also useful for controlled and targeted drug delivery.

7. Proposed work Plan/ Formulation and Structure of Study:

Year-wise Plan of work and targets to be achieved:

Sr. No.	Work	Duration Of Work
1.	Extensive Literature Survey	6 Months
2.	Selection And Collection Of Drug And Excipients	3 Months
3.	Preformulation Studies	3 Months
4.	Formulation Development And Optimization Of Nanosponges	8 Months
5.	Evaluation Of Optimized Formulation	8 Months
6.	Statistical Analysis, Data Interpretation And Conclusions	3 Months
7.	Communication With Research Journals & Publishing Data	3 Months
8.	Thesis writing	2 Months
Total duration of work		**36 Months**

8. References:

1. Satyajit Panda, Sv Vijayalakshmi, Snigdha Pattnaik, Ranjit Prasad Swain, "Nanosponges: A Novel Carrier For Targeted Drug Delivery", International Journal Of Pharmatech Research, 2015, Volume-8, 213-224.

2. Madhuri Shringirishi, Sunil Kumar Prajapati, Alok Mahor, Shashi Alok, Poonam Yadav, Amita Verma, "Nanosponges: A Potential Nanocarrier For Novel Drug Delivery-A Review", Asian Pacific Journal Of Tropical Disease, 2014, Elsevier Publication, 4(Suppl 2): S519-S526.

3. Bezawada S., Charanjitha, Reddy V.M., Naveena, Gupta V.R., "Nanosponges: A Concise Review For Emerging Trends", International Journal Of Pharmaceutical Research And Biomedical Analysis, 2014, Volume-3, 1-6.

4. Jilsha G., Vidya Viswanand., "Nanosponge A Novel Approach Of Drug Delivery System", International Journal Of Pharm. Science Review And Research 2013,19(2).

5. Balasaheb M. T., Patil P. M., Jahagirdar A. C., Khandekar D. B., "Nanosponge An Emerging Drug Delivery System", International Journal Of Institutional Pharmacy And Life Sciences,2015, 5(6).

6. Vishwakarma A., Nikam P., Mogal R., Talale S., "Nanosponges A Benifiaction For Novel Drug Delivery System", Int. Jour. Pharm. Tech Sciences,2014, 6(1).

7. Selvamuthukumar Subramanian, Anandam Singiredd, Kannan Krishnamoorthy, And Manavalan Rajappan, "Nanosponges: A Novel Drug Delivery System-Review", J Pharm Pharmaceut Sci (Www.Cspscanada.Org) 2012, 15(1), 103 -111.

8. B. Indira, Sai Santosh Bolisetti, Ch. Samrat, Sama Mallikarjun Reddy, Neerudu Srikanth Reddy, " Nanosponges: A New Era In Drug Delivery: Review", Journal Of Pharmacy Research, Volume 5, Issue 11, 2012, 5293-5296.

9. E. K. Patel, And R. J. Oswal, "Nanosponge And Micro Sponges: A Novel Drug Delivery System", International Journal Of Research In Pharmacy And Chemistry, Ijrpc 2012, 2(2) Issn: 2231-2781, 237-244.

10. Trotta F., Tumiatti V., Cavalli R., Rogero C., Mognetti B., Berta G., "Cyclodextrin-Based Nanosponges As A Vehicle For Anti-Tumoral Drugs", 2009, Wo 2009/003656 A1.

11. Nacht S, Kantz M.; (1992) "The Microsponge: A Novel Topical Programmable Delivery System, In: Topical Drug Delivery Systems", David W.O And Anfon H.A (Ed), 42.

12. Kundlas J., Nautiyal U., Jassal M. "Nanosponges: As Originated Form For Targeted Drug Delivery", International Journal Of Recent Advances In Pharmaceutical Research, April- 2015; 5(2): 75-81.

13. Uday B.B., Manvi F.V., Kotha R., Pallax S.S., Paladugu A. And Reddy K.R., "Recent Advances In Nanosponges As Drug Delivery System", International Journal Of Pharmaceutical Sciences And Nanotechnology, Volume-6, April-June 2013;1934-1944.

14. Subramanian S, Singireddy A, Krishnamoorthy K, Rajappan M. "Nanosponges: A Novel Class of Drug Delivery System-Review". J Pharm Pharm Sci 2012; 15(1): 103-111.

15. Swaminathan S, Darandale S, Vavia Pr., "Nanosponge-Aided Drug Delivery: A Closer Look", Pharm Formul Qual 2012; 12-15.

16. Vavia P.R., Swaminathan S, Trotta F, Cavalla R., "Application Of Nanosponges In Drug Delivery", In: Proceedings Xiii International Cyclodextrin Symposium; 2006 May 14-17; Turin, Italy. Berlin: Springer; 2006. P. 207.

17. Rana Z Ahmed., Gunjan, Patil, And Zahid Zaheer "Nanosponge – A Completely New Nano-Horizon: Pharmaceutical Applications And Recent Advances", Drug Dev Ind Pharm. 2012 Jun 11. Pmid 22681585.

18. H.V. Gangadharappa, Sarat M. Chandra Prasad, Rudra Pratap Singh, "Formulation, In Vitro And *In Vivo* Evaluation Of Celecoxib Nanosponge Hydrogels For Topical Application", Journal Of Drug Delivery Science And Technology, 2017, 1-30.

19. Prathima Srinivas, Sreeja. K, "Formulation And Evaluation Of Voriconazole Loaded Nanosponges For Oral And Topical Delivery", International Journal Of Drug Development & Research, 2013, 5(1), 55-69.

20. Patil Bhagyashree Subhash And S. K. Mohite, " Formulation Design & Development Of Artesunate Nanosponge", European Journal Of Pharmaceutical And Medical Research, *2016,3(5),* 206-211.

21. Khalid A. Ansari, Pradeep R. Vavia, Francesco trotta, Robert Cavalli, "Cyclodextrin-Based Nanosponges for Delivery of Resveratrol: In Vitro Characterisation, Stability, Cytotoxicity and Permeation Study", AAPS PharmScitech, 2011, Vol 12, 279-286.

22. Renuka Sharma And Kamla Pathak, "Polymeric Nanosponges As An Alternative Carrier For Improved Retention Of Econazole Nitrate Onto The Skin Through Topical

Hydrogel Formulation", Pharmaceutical Development And Technology, 2011,16(4), 367-376.

23. G. Jilsha And Vidya Viswanad, " Nanosponge Loaded Hydrogel Of Cephalexin For Topical Delivery", International Journal Of Pharmaceutical Sciences And Research, *2015*, Vol. 6(7): 2781-2789.

24. Madhuri Shringirishi, Alok Mahor, Rishikesh Gupta, Sunil Kumar Prajapati, Kuldeep Bansal, Prashant Kesharwani, "Fabrication And Characterization Of Nifedipine Loaded B-Cyclodextrin Nanosponges: An *In Vitro* And *In Vivo* Evaluation", Journal Of Drug Delivery Science And Technology, 41 (2017) 344-350.

25. David Lembo, Shankar Swaminathan, Manuela Donalisio, Andrea Civra, Linda Pastero, Dino Aquilano, Pradeep Vavia, Francesco Trotta, Roberta Cavalli, "Encapsulation of Acyclovir in new carboxylated cyclodextrin-based nanosponges improves the agent's antiviral efficacy", International Journal of Pharmaceutics, Elsevier publication, 443 (2013) 262– 272.

26. S. Swaminathan, P. Vavia, F. Trotta and S. Torne, "Formulation of beta-cyclodextrin based nanosponges of Itraconazole", J. Incl. Phenom. Macrocycl. Chem., 2007; 57: 89–94.

27. Cavalli R, Trotta F. Tumiatti W. Cyclodextrin-based nanosponges for drug delivery, J. Incl. Phenom. Macrocycl. Chem 2006; 56: 209–213.

28. Swaminathan S, Vavia PR, Trotta F, Torne S. Formulation Of Beta cyclodextrin Based Nanosponges Of Itraconazole. J Incl phenom Macrcycl Chem 2007; 57(1-4): 89-94.

Name of Research Candidate **Signature**	Mr. Shaikh Nasheer Shadulla
Remarks of The Guide	
Name and Designation of Research Supervisor **Signature**	**Dr. Nagoba S. N.** **Associate Professor and Head**, Department of Pharmaceutics, Channabasweshwar Pharmacy College (Degree), Latur.
Remarks of Director/ Principal/ Head of The School/ Institution **Signature**	**Dr. S. G. Gattani** **Director,** School of Pharmacy, S.R.T.M.University, Nanded. (Seal of The School/Institute)